

# PATENT COOPERATION TREATY

# PCT

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## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>431WO</b>	<b>FOR FURTHER ACTION</b> <span style="float: right;">See Form PCT/PEA/416</span>	
International application No. <b>PCT/DK2004/000290</b>	International filing date (day/month/year) <b>27.04.2004</b>	Priority date (day/month/year) <b>30.04.2003</b>
International Patent Classification (IPC) or national classification and IPC <b>C07C323/20, C07D207/12, C07D207/16, C07D211/46, C07D211/60, A61K31/198, A61P25/18</b>		
Applicant <b>H. LUNDBECK AS et al</b>		
1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of 6 sheets, including this cover sheet. 3. This report is also accompanied by ANNEXES, comprising: a. <input type="checkbox"/> sent to the applicant and to the International Bureau a total of sheets, as follows: <input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). <input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box. b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).		
4. This report contains indications relating to the following items: <div style="margin-left: 20px;"> <input checked="" type="checkbox"/> Box No. I      Basis of the opinion  <input type="checkbox"/> Box No. II     Priority  <input checked="" type="checkbox"/> Box No. III    Non-establishment of opinion with regard to novelty, inventive step and industrial applicability  <input type="checkbox"/> Box No. IV    Lack of unity of invention  <input checked="" type="checkbox"/> Box No. V     Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement  <input type="checkbox"/> Box No. VI    Certain documents cited  <input type="checkbox"/> Box No. VII    Certain defects in the international application  <input type="checkbox"/> Box No. VIII   Certain observations on the international application                 </div>		
Date of submission of the demand  <b>24.09.2004</b>	Date of completion of this report  <b>22.03.2005</b>	
Name and mailing address of the international preliminary examining authority:   European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer  English, R  Telephone No. +31 70 340-2860  	

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/DK2004/000290

**Box No. I Basis of the report**

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
    - ☐ international search (under Rules 12.3 and 23.1(b))
    - ☐ publication of the international application (under Rule 12.4)
    - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements**\* of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

**Description, Pages**

1-72 as originally filed

**Claims, Numbers**

1-21 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
    - ☐ the description, pages
    - ☐ the claims, Nos.
    - ☐ the drawings, sheets/figs
    - ☐ the sequence listing (*specify*):
    - ☐ any table(s) related to sequence listing (*specify*):
  4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
    - ☐ the description, pages
    - ☐ the claims, Nos.
    - ☐ the drawings, sheets/figs
    - ☐ the sequence listing (*specify*):
    - ☐ any table(s) related to sequence listing (*specify*):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/DK2004/000290

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 21

because:

☒ the said international application, or the said claims Nos. 21 relate to the following subject matter which does not require an international preliminary examination (specify):

**see separate sheet**

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/DK2004/000290

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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	1-21
	No: Claims	
Inventive step (IS)	Yes: Claims	1-21
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-20
	No: Claims	

2. Citations and explanations (Rule 70.7):

**see separate sheet**

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claim 21 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(I) PCT).

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Reference is made to the following document:

**D1:** WO 03/000646 A (PFIZER PRODUCTS) 3 January 2003

**1. Subject-matter**

The present application concerns aromatic oxyphenyl and sulphanylphenyl amino acid derivatives, which are glycine transporter inhibitors, and their use in the treatment of disorders in the CNS such as schizophrenia.

**2. Novelty**

Document D1 describes certain N-(3-phenyl-3-phenoxypropyl)sarcosine derivatives and their use as inhibitors of glycine transport in the treatment of schizophrenia and other conditions. These compounds differ from those of the present application in that they contain an additional substituted phenylmethylene group ( $\text{YC}_6\text{H}_4\text{CH}$  not present in the latter. Consequently, the subject-matter of claim 1, dependent claims 2-18 and independent claims 19-21 (which concern the use of compounds of claim 1) is considered to be new and to satisfy the requirements of Article 33(2) PCT.

**3. Inventive step**

The document D1 is regarded as being the closest prior art to the subject-matter of claims 1, 19-21, and discloses the use of certain N-(3-phenyl-3-phenoxypropyl)-sarcosine derivatives as inhibitors of glycine transport in the treatment of schizophrenia and other conditions. As noted above these compounds differ from

those of the present application in that they contain an additional phenylmethylene group.

According to D1 the prior-art compounds have  $IC_{50}$  values for the inhibition of glycine reuptake of less than 10  $\mu$ M (page 16, lines 2-4) whilst for the compounds of the present application the  $IC_{50}$  value for the inhibition of glycine uptake is also less than 10  $\mu$ M (i.e. 10,000 nM, page 70, lines 31-32). Thus, the compounds of the present application have a similar activity to those of the prior art.

The problem to be solved by the present invention may therefore be regarded as the provision of alternative glycine transporter inhibitors. The applicant solves this problem by means of the aromatic oxyphenyl and sulphonylphenyl amino acid derivatives of claim 1. There is no indication in D1 or anywhere else in the prior art that removal of the substituted phenylmethylene group of the compounds of D1 to form the compounds of the present application would lead to compounds which are capable of inhibiting glycine transport. Consequently, the subject-matter of claims 1, 19-21 and dependent claims 2-18 can be considered to involve an inventive step and to satisfy the requirements of Article 33(3) PCT.

#### **4. Industrial applicability**

For the assessment of the present claim 21 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognise as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.